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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,040	12/30/2005	Brian G. Van Ness	09531-109US1	9035

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
12/04/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/532,040	VAN NESS ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-29* is/are pending in the application.

4a) Of the above claim(s) *9-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/5/09 has been entered. Applicant's amendment and response received with the RCE on 10/5/09 has also been entered. Claim 2 has been canceled. Claims 1, and 3-29 are pending in the instant application.

The previous office action acknowledged that applicant had elected without traverse the invention of Group I, and the species Bcl-xl in the responses received on 2/26/08 and 5/28/08. Claims 9-29 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, and 3-8 are therefore currently under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Claim Rejections - 35 USC § 112

The rejection of claims 1 and 3-8 under 35 U.S.C. 112, first paragraph, for scope of enablement is withdrawn in view of applicant's amendments to the claims which limit the invention to the previously identified scope of enablement.

Claim Rejections - 35 USC § 103

The rejection of previously pending claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Grillot et al. (1996) J. Exp. Med., Vol. 183, 381-391, in view of Adams et al. (1985) Nature, Vol. 318, 533-538, is maintained over claims 1 and 3-8, and withdrawn over canceled claim 2. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that the rationale for combining the teachings of the cited references does not apply as substitution of the kappa enhancer for the heavy chain enhancer is not a simple substitution of one known element for another with predictable results. According to applicant, the kappa enhancer is active at different times than the heavy chain enhancer in B cell development and further argues that the unlike the kappa enhancer which is active in plasma cells, the heavy chain enhancer leads to earlier B cell malignancies, citing Fulton and Van Ness (1993) and (1994), both made of record in the IDS of 10/6/06. The applicant also states that oncogene transformation of plasma cells required the combination of an Ig promoter with the kappa enhancer. Finally, the applicant reiterates their argument Adams teaches away from using the kappa enhancer by teaching that the heavy chain enhancer resulted in higher tumor incidence that the kappa enhancer.

In response, Fulton and Van Ness (1993) discuss differences between the two known kappa light chain enhancers and explore the activity of these two light chain enhancers in the context of different promoters in B cells at different developmental stages. Fulton and Van Ness

(1993) do not discuss or provide data using any heavy chain promoter. It is acknowledged that Fulton and Van Ness (1993) show that the 3' kappa enhancer is more active in mature and plasma type B cells, versus pre-B cells; however, nothing in this reference speaks to why one of ordinary skill in the art would not have found the kappa enhancer substitutable for the heavy chain enhancer. Fulton and Van Ness (1994) does look at the activities of both the heavy chain enhancers and the light chain enhancers. However, the data provided by Fulton and Van Ness (1994) does not support applicant's position. Fulton and Van Ness clearly show that the activity of the heavy chain intron enhancer, the μ enhancer, is substantial in both mature and plasma type cells (Fulton and Van Ness (1994), page 4218, Figures 1 and 2). According to the data provided by Fulton and Van Ness (1994), both the heavy chain μ enhancer and the kappa 3'enhancer are active in mature B cells and in plasma cells.

Regarding the development of different types of B cell malignancies, the applicant is reminded that the transgenic mouse as claimed does not contain any limitation regarding tumor development. The only phenotype recited in the claims as written states that the transgenic mouse "..exhibits expanded plasma cell and mature B cell populations compared to a corresponding wild-type mouse". In addition, none of claims 1 and 3-7, requires a kappa promoter. It is also noted that neither Fulton and Van Ness (1993) or (1994) teach anything regarding the transformative properties of any of the heavy chain or light chain enhancers in any type of B cell.

Finally, regarding the argument, reiterated from applicant's previous response, that Adams teaches away from using the kappa enhancer by teaching that the heavy chain enhancer resulted in higher tumor incidence that the kappa enhancer, the previous office action responded

that Grillot et al. only differs from the claimed invention by using an Ig heavy chain enhancer instead of an Ig kappa 3' enhancer. Adams et al. was cited to supplement the teachings of Grillot et al. by teaching that both the Ig heavy chain enhancer and the Ig kappa chain enhancer are effective in driving B cell specific heterologous transgene expression in transgenic mice (Adams et al., pages 533-534 and 537). As such, since the Ig kappa chain enhancer, like the Ig heavy chain enhancer, is capable of directing B cell specific expression of heterologous transgenes in transgenic mice, it would have been *prima facie* obvious to the skilled artisan at the time of filing to substitute the Ig kappa enhancer taught by Adams et al. for the Ig heavy chain enhancer in the constructs for making a transgenic mouse according to Grillot et al. with a reasonable expectation of success in using such a construct to produce a transgenic mouse exhibiting a phenotype of expanded mature B cells and plasma cell populations, as such a replacement represents nothing more than simple substitution of one known element for another to obtain predictable results. The functional similarity referred to in previous office actions was the clear demonstration by Adams that both the heavy chain and kappa chain enhancer effectively drive B cell specific heterologous transgene expressing in transgenic mice. The rejection of record did not state or imply that the level of enhancer activity of the heavy chain and kappa enhancer was equivalent or identical, and the rejection of record is not predicated upon equivalent or identical levels of activity. As stated in the previous office action, the motivation to combine the teachings of the cited references need not be supported by a finding that the prior art suggested that the combination claimed by the applicant was the preferred, or most desirable combination over the other alternatives. *In re Fulton*, 391 F.3d 1195, 73 USPQ2d 1141 (Fed. Cir. 2004).

As such, applicant's arguments are not found persuasive and the rejection of record stands.

The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Grillot et al. (1996) J. Exp. Med., Vol. 183, 381-391, in view of Adams et al. (1985) Nature, Vol. 318, 533-538, applied to claims 1 and 3-7 above, and further in view of Miller et al. (1992) Immunogenetics, Vol. 35, 24-32 is maintained. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant reiterates their arguments regarding the teachings of Grillot et al. and Adams et al. and further states that Miller et al. does not overcome the deficiencies of Grillot et al. and Adams et al. In response, the arguments regarding the teachings of Grillot et al. and Adams et al. have been discussed in detail above and have not been found persuasive in overcoming the rejection of record. Therefore, the rejection stands.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center

fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633